

Brain Disorders in the Developing World: Research across the Lifespan

This RFA solicits applications to plan and develop collaborative research and capacity-building projects on brain disorders throughout life relevant to low- and middle-income nations. Applicants will develop innovative collaborative research programs that will contribute to building sustainable research capacity in neurological/neurodevelopmental (including sensory, motor, cognitive, and behavioral) impairment.

This first phase of the "Brain Disorders in the Developing World: Research across the Lifespan" initiative will consist of two-year planning/development grants using the R21 grant mechanism. The R21 grant will provide support to initiate preliminary studies and to organize, plan, prepare, and assemble an application for a more comprehensive R01 grant involving collaboration between high-income and low- to middle-income country investigators and incorporating both research and capacity building. An RFA for the second competitive phase of this initiative is currently planned to be issued in fiscal year 2005. The main goals for this application are to assess needs, develop collaborations and needed resources, show feasibility, and generate preliminary data for the collaborative research to be proposed in a follow-up R01 submission.

The applicants should propose specific milestones and a timeline to meet these goals. Efforts must include pilot research projects to demonstrate feasibility of the research approaches and develop further research directions. Training, informal meetings, workshops, and small conferences may be part of the plan. New analyses of extant data sets and development or use of new methodologies or approaches may also be proposed.

Each exploratory grant should also present a description of the anticipated longer-term goals of the collaboration as it develops into an application for an R01 research grant with capacity building and training built in. As one outcome of the work under the R21 grant, grantees will be expected to provide a detailed assessment of the specific research issues and capacity-building and training needs in the developing country that the proposed follow-up R01 or other future application will address. The relevance of the focus of the proposed research to the health of the host endemic country should be justified. The assessment may include, but is not limited to, needed skills and expertise in laboratory, clinical, epidemiological, and social science research. In addition, the involvement, if any, of the developing country institution and faculty in formulating treatment and prevention policies locally, nationally, regionally, or internationally should be noted.

The applicants will also initiate development of needed resources and infrastructure. Research training in the context of the proposed research may take place at any of the collaborating sites and may vary, depending on the strengths of the particular investigators and institutions that apply and the need to build capacity to support research and future interventions. However, any research at the high-income site must also involve training for participating low- to middle-income investigators, and more than 50% of the proposed research must be conducted at the low- to middle-income country site(s).

Relevant research for the R21 and follow-up applications may range from basic science to epidemiological, translational, clinical, operational, and health services research that is culturally appropriate, feasible, and acceptable for implementation within the foreign site. Relevant research topics should be related to neurodevelopmental disabilities

and neurological disorders, including cognitive, motor, sensory, and behavioral impairment from birth to advanced age. Examples include mental retardation, seizure disorders such as epilepsy, movement disorders such as Parkinson disease, and dementias (including those related to age and those caused by HIV, malaria, or other infection).

This RFA encourages development of multidisciplinary research whenever relevant to the research question. Expertise may involve, but is not limited to, fields such as neurology, cognitive neuroscience (including functional brain imaging), developmental neurobiology, neurotoxicology, neuroendocrinology, pharmacology, psychiatry, neuroimmunology, neurovirology, and biotechnology (e.g., for development of diagnostic tools), as well as the behavioral and social sciences. Examples of some cross-cutting areas for research are ethnographic studies and other areas of social science, particularly to address health systems and appropriate interventions within a given society or group, and research focusing on gender and socioeconomic factors in the etiology and treatment of the disorders to be addressed.

Suggested areas of research include, but are not limited to: 1) descriptive epidemiology to describe and define the problem in the countries in question by assessing needs and determining the magnitude and factors involved in the problem to be addressed; 2) analytical epidemiology to identify potential etiological factors in the populations of interest, including factors responsible for predispositions to the neurological consequences of various infections, infestations, and/or neurotoxins; 3) genetic factors throughout life, beginning in the prenatal period, that result in cognitive, behavioral, motor, or sensory impairment or disorders; 4) natural history of common neurological diseases/disorders and the influence of sociocultural or other environmental variables that impact upon this course; 5) research on multiple insults, especially common in the developing world; 6) environmental factors across the lifespan, beginning in the prenatal period, that result in cognitive, behavioral, motor, or sensory impairment; 7) factors affecting cognitive, emotional, and physical health and survival in older persons; 8) research on other factors that affect healthy brain development, such as access to appropriate health care, availability of resources, preventive or screening practices, etc.; and 9) research on potential interventions and how the success or failure of interventions may be modulated by sociocultural and gender variables.

For information on the specific research interests of the RFA sponsors and other details of this program, please consult the full text of the announcement, available online at <http://grants1.nih.gov/grants/guide/rfa-files/RFA-TW-03-007.html>. Applicants for this R21 award may request direct costs of up to \$100,000 per year, in increments of \$25,000, for a maximum of two years. The funded R21 grants will not be renewable.

Applications must be prepared using the PHS 398 research grant application instructions and forms (rev. 5/2001). The PHS 398 is available at <http://grants.nih.gov/grants/funding/phs398/phs398.html> in an interactive format. The deadline for letters of intent is 11 February 2003, with final applications due 11 March 2003.

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Morris K. Udall Parkinson's Disease Research Centers of Excellence

In response to continuing research progress and opportunity, and in recognition of continuing congressional interest in intensifying and expanding basic and clinical research in Parkinson's disease (PD), the National Institute of Neurological Disorders and Stroke and the NIEHS invite qualified investigators to submit grant applications for the establishment of Morris K. Udall Parkinson's Disease Research Centers of Excellence. These centers will encourage additional research opportunities and discoveries that will lead to improved diagnosis and treatment of patients with PD and related neurodegenerative disorders, based on a better understanding of the fundamental cause(s) of the disease. It is expected that these centers will form a consortium of investigators that will foster an environment that will enhance research effectiveness in a multidisciplinary setting, utilizing specialized methods relevant to the study of these disorders.

Each center may conduct either basic or clinical research, or proportions of each that are appropriate for the research objectives. Emphasis is placed on multidisciplinary and collaborative studies that can best be carried out in a center setting. The organizational structure of the center should be flexible to allow the expeditious translation of new scientific findings and technological developments to clinical research. Studies might include, but are not limited to, the epidemiology, natural history, pathogenesis, or treatment of PD and related disorders. To generate new ideas, develop young investigators, and enhance the national PD research infrastructure, each center should have a research training component identifying opportunities for either basic or clinical interinstitutional research collaborations. Centers are expected to be characterized by a broad but thematically coherent set of investigations bearing on the etiology, pathogenesis, and treatment of PD. To the extent that they inform and/or expand research on PD, investigations on related neurodegenerative disorders may be included.

It is anticipated that the ensemble of individual centers will constitute a comprehensive and systematic pursuit of the needs and opportunities in PD research. Each single center will focus on a select subset of topics according to its individual strengths while continuing to expand the PD research enterprise through collaborations. To facilitate interaction and collaboration between the centers, a consortium will be established.

New research techniques have created extraordinary opportunities for further exploration into the etiology, pathogenesis, diagnosis and treatment of PD and related neurodegenerative disorders. Topics of investigation within a center might include, but are not limited to, 1) clinical studies of PD, parkinsonism, and related disorders; 2) the natural history of PD and related disorders including prospective clinical assessment, neuropathological analysis, and banking of brain tissue from individuals with PD who agree to participate in an autopsy program; 3) studies to address the nonmotor aspects of PD; 4) development of therapeutic technology related to PD; 5) epidemiological and genetic studies to identify risk and susceptibility factors; 6) studies on gene-environment interactions as risk factors for PD; 7) translational research; 8) cellular and molecular mechanisms of cell injury and death in PD and related neurodegenerative disorders; 9) studies of the structure, function, composition, role, and possible interrelationship of proteins and inclusion bodies implicated in the pathogenesis of PD and related disorders; 10) development of animal models and

their use for investigation of pathophysiology and efficacy of therapeutic intervention; 11) development and function of the neural circuitry involved in PD and related disorders, including those functions affected by the disease process or treatment; 12) molecular and cell biology of the dopaminergic systems and other relevant neurotransmitters and neuromodulators and their function in the brain; 13) exploration of trophic factors and their receptors that promote the survival of dopamine neurons in the adult brain; 14) neuronal reconstruction using engineered cell lines that are relevant to PD; and 15) markers of PD onset, progression, and response to therapy.

The mechanism of support for the Morris K. Udall Parkinson's Disease Research Centers of Excellence is the Research Center Grant (P50). Because the nature and scope of the research proposed in response to this PA may vary, it is anticipated that the size of the award may also vary. It is expected that grants will not exceed \$1 million per year direct costs for five years.

Applications must be prepared using the PHS 398 research grant application instructions and forms (rev. 5/2001). The PHS 398 is available at <http://grants.nih.gov/grants/funding/phs398/phs398.html> in an interactive format. Applications submitted in response to this PA will be accepted at the standard application deadlines, which are available at <http://grants.nih.gov/grants/dates.htm>. Complete information on this announcement is available at <http://grants1.nih.gov/grants/guide/pa-files/PA-03-004.html>.

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Continued Development and Maintenance of Bioinformatics/Computational Biology Software

Biomedical research laboratories occasionally create software to solve a problem the laboratory faces. These software packages sometimes evolve into a well-designed system that can be easily extended and that is useful to a much broader community beyond the members of the originating laboratory. The goal of this PA is to support the continued development, maintenance, testing, and evaluation of existing software. The proposed work should apply best practices and proven methods for software design, construction, and implementation to extend the applicability of existing bioinformatics-computational biology software to a broader biomedical research community.

This initiative pertains to bioinformatics/computational biology software that is recognized to perform an important function in furthering biomedical research. The software should perform reliably and precisely according to the computing demands of end users. The algorithms that are employed by the software should be well documented, as should be the underlying assumptions of these algorithms to prevent potential misuse.

Contemporary software must be fully documented and easy to modify and extend. Defects that arise in any software must be correctable with limited effort. As the needs of a community of users change,

the software that supports their research efforts must be easily modified. Reparability and evolvability are particularly important because the scientific discovery process is open-ended and ever-changing. Interoperability and portability are also a major concern. Where appropriate, software applications should operate on a variety of platforms employing different operating systems.

Awards made under this PA will support continued software development, evaluation, and testing of preexisting bioinformatics/computational biology software for data management and analysis, computational biology, and modeling and simulation. Support will be provided for porting software to new platforms and operating systems as well as the costs associated with maintaining the software as existing operating systems change. The proposed software should not substantially duplicate another software package that is already in wide use.

This PA will use the NIH R01 award mechanism as well as competitive supplements to existing R01, R33, P01, P41, P50, and P60 grants that have already been awarded by one of the participating institutes or centers. Applications for competitive supplements cannot extend beyond the parent project period of performance, and must have the same principal investigator.

Applications must be prepared using the PHS 398 research grant application instructions and forms (rev. 5/2001). The PHS 398 is available at <http://grants.nih.gov/grants/funding/phs398/phs398.html> in an interactive format. Applications submitted in response to this PA will be accepted at the standard application deadlines, available at <http://grants.nih.gov/grants/dates.htm>. Application deadlines are also indicated in the PHS 398 application kit.

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